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WE CLAIM:

1. A DNA plasmid comprising an adenoviral gene or gene region that encodes a cytotoxic protein operably linked to an inducible promoter.

2. The DNA plasmid of claim 1 wherein said adenoviral gene or gene region is selected from the E2A gene or E4 gene region.

3. A DNA plasmid comprising an adeno-associated viral gene that encodes a protein operably linked to an inducible promoter.

4. The DNA plasmid of claim 3 wherein said adeno-associated viral gene is selected from the rep gene region and cap gene region.

5. A DNA plasmid comprising an adeno-associated viral gene wherein said gene encodes one of the adeno-associated virus Rep proteins and is operably linked to an inducible promoter.

6. The DNA plasmid of any one of claims 1-5 in the alternative wherein said inducible promoter is the promoter from the cAMP response element binding protein regulated genes.

7. The DNA plasmid of any one of claims 1-5 in the alternative wherein said inducible promoter is selected from the gene encoding mammalian alpha inhibin.

8. The DNA plasmid of any one of claims 1-5 in the alternative wherein said inducible promoter is selected from the gene encoding mouse alpha inhibin.

9. The DNA plasmid of any one of claim 1 wherein said inducible promoter is selected from the gene encoding the tetracycline responsive promoter.

10. The plasmid pIK6.1 MIP(α)-E4 designated ATCC #75879.

11. A packaging cell line that supports the growth of a mutant adenovirus defective in replication, wherein said adenovirus comprises at least two deletions, at least two mutations, or at least one mutation and one deletion selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and optionally a deletion of the E3 gene region.

12. A packaging cell line that supports the growth of a recombinant adenoviral vector, wherein said vector comprises at least two deletions, two mutations or one deletion and one mutation selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and optionally a deletion of the E3 gene region and said recombinant adenoviral vector additionally comprises a transgene that replaces any one of said deletions.

13. A packaging cell line that supports the growth of a mutant adeno-associated virus defective in replication, wherein said packaging cell line comprises the E1, E2A and E4 early gene regions, the DNA sequences
5 encoding the virus-associated RNA, and wherein said virus is free of helper adenovirus.

14. A packaging cell line that supports the growth of a recombinant adeno-associated virus defective in
10 replication grown in a packaging cell line comprising the E1, E2A and E4 early regions, and virus-associated RNA sequences, wherein said virus is free of helper adenovirus.

15. A packaging cell line that supports the growth of a mutant adeno-associated virus defective in
15 replication, said packaging cell line comprises E1, E2A, E4 early gene regions, virus-associated RNA sequences, adeno-associated virus rep gene region, and optionally the E3 early gene region, and wherein said mutant virus carries a
20 deletion of adeno-associated virus rep gene region and is free of helper adenovirus.

16. A packaging cell line that produces a recombinant adeno-associated virus defective in replication,
25 wherein said packaging cell line comprises E1, E2A, E4 early gene regions, DNA sequences encoding virus-associated RNA, adeno-associated virus rep gene region, and optionally the E3 early region, and wherein said mutant virus carries a
30 deletion of adeno-associated virus rep gene region and is free of helper adenovirus.

17. A packaging cell line that supports the growth of a mutant adeno-associated virus defective in replication, wherein said packaging cell line comprises E1, E2A, E4 early gene regions, virus-associated RNA sequences, adeno-associated virus rep gene region, adeno-associated virus cap gene region and optionally the E3 early gene region, and wherein said mutant virus carries a deletion of adeno-associated virus rep gene region and is free of helper adenovirus.

18. A packaging cell line that produces a recombinant adeno-associated virus defective in replication, wherein said packaging cell line comprises E1, E2A, E4 early gene regions, DNA sequences encoding virus-associated RNA, adeno-associated virus rep region, the adeno-associated virus cap gene region and optionally the E3 early region, and wherein said mutant virus carries a deletion of adeno-associated virus rep gene region and is free of helper adenovirus.

19. A mutant adenovirus defective in replication, wherein said adenovirus comprises at least two deletions, at least two mutations, or at least one mutation and one deletion selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and optionally a deletion of the E3 gene region, and wherein said adenovirus is produced in the packaging cell line of claim 11.

20. A mutant adenovirus defective in replication, wherein said adenovirus comprises at least two deletions, at least two mutations, or at least one mutation and one
5 deletion selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and optionally a deletion of the E3 gene region.

21. A recombinant adenoviral vector, wherein said
10 vector comprises at least two deletions, two mutations or one deletion and one mutation selected from the group consisting of E1, E2A, E4 early gene regions, viral structural gene sequences, and optionally a deletion of the E3 gene region, wherein said recombinant adenoviral vector
15 additionally comprises a transgene that replaces any one of said deletions, said vector is produced from the packaging cell line of claim 12.

22. A recombinant adenoviral vector, wherein said
20 vector comprises at least two deletions, two mutations or one deletion and one mutation selected from the group consisting of E1, E2A, E4 early gene regions, viral structural genes, and optionally a deletion of the E3 gene region, wherein said recombinant adenoviral vector
25 additionally comprises a transgene that replaces any one of said deletions.

23. A mutant adeno-associated virus defective in replication grown in a packaging cell line, wherein said
30 packaging cell line comprises the E1, E2A and E4 early gene regions, and the DNA sequences encoding virus-associated RNA, and wherein said virus is free of helper adenovirus.

24. A recombinant adenoviral vector defective in replication grown in a packaging cell line, wherein said packaging cell line comprises the E1, E2A and E4 early gene regions, the virus-associated RNA sequences, and optionally the E3 early gene region, and wherein said virus is free of helper adenovirus.

25. A mutant adeno-associated virus defective in replication grown in a packaging cell line, wherein said packaging cell line comprises E1, E2A, E4 early gene regions, the DNA sequences encoding virus-associated RNA, adeno-associated virus rep gene region, and optionally the E3 early gene region, and said mutant virus comprises a deletion of adeno-associated virus rep gene region and is free of helper adenovirus.

26. A recombinant adeno-associated viral vector defective in replication grown in a packaging cell line, wherein said packaging cell line comprises E1, E2A, E4 early gene regions, the DNA sequences encoding virus-associated RNA, adeno-associated virus rep gene region, and optionally the E3 early region, wherein said viral vector carries a deletion of adeno-associated virus rep gene region and is free of helper adenovirus, and additionally comprises a transgene that replaces said deletion.

27. A mutant adeno-associated virus defective in replication grown in a packaging cell line, wherein said packaging cell line comprises E1, E2A, E4 early gene regions, the DNA sequences encoding virus-associated RNA, adeno-associated virus rep gene region, the adeno-associated virus cap gene region and optionally the E3 early gene region, and said mutant virus carries a deletion of adeno-associated virus rep gene region and is free of helper adenovirus.

28. A recombinant adeno-associated viral vector defective in replication grown in a packaging cell line, wherein said packaging cell line comprises E1, E2A, E4 early gene regions, the DNA sequences encoding virus-associated RNA, adeno-associated virus rep gene region, adeno-associated virus cap gene region and optionally the E3 early region, said viral vector carries a deletion of

adeno-associated virus rep gene region and is free of helper adenovirus, and additionally comprises a transgene that replaces said deletion.

29. A method of infecting a mammalian target cell with a recombinant adenovirus or adeno-associated virus containing a transgene, said method comprising the steps of:

- i. infecting said target cell with a recombinant viral vector of any one of claims 21, 22, 24, 26 or 28 in the alternative, said viral vector carrying a selected transgene and,
- ii. expressing said transgene in the targeted cell.

30. Mammalian target cells infected with a transgene produced by the method of claim 29.

31. The target cells of claim 30 wherein said cells are selected from the group consisting of replicating, slow-replicating or non-replicating human cells.

5 32. The packaging cell line derived from human embryonic kidney cells given the ATCC designation #CRL 11711. *release*

10 33. A method of treating a hereditary or acquired disease, said method comprising the steps of:

- 15 i. administering a pharmaceutically acceptable dose of a recombinant adenoviral derived- or adeno-associated viral derived- vector of any one of claims 21, 22, 24, 26, or 28 in the alternative, in a target cell, wherein said vector comprises a transgene wherein said transgene is a therapeutic gene, and
- 20 ii. expressing said therapeutic gene in the target cell such that the hereditary or acquired disease is ameliorated.

25 34. A vaccine comprising a recombinant adenoviral derived or adeno-associated viral derived vector of any one of claims 21, 22, 24, 26, 28, 36, 55, 57, 59, 60 or 62 in the alternative, and a pharmaceutically acceptable carrier.

30 35. A packaging cell line that supports the growth of an adenoviral vector, wherein said vector comprises at least two deletions selected from the group consisting of E1 and E4 early gene regions and optionally a deletion of the E3 gene region, wherein said recombinant adenoviral vector additionally comprises a transgene that replaces any one of said deletions.

36. A recombinant adenoviral vector, wherein said vector comprises at least two deletions selected from the group consisting of E1 and E4 early gene regions, and optionally a deletion of the E3 gene region, wherein said recombinant adenoviral vector additionally comprises a transgene that replaces any one of said deletions.

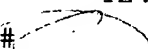
37. A DNA plasmid comprising an adenoviral gene fragment E4 open reading frame ORF6 operably linked to an inducible promoter.

38. The DNA plasmid of claim 37 wherein the inducible promoter is a promoter selected from the cAMP response element binding protein regulated genes.

39. The DNA plasmid of claim 38 wherein the inducible promoter is selected from the gene encoding mammalian alpha inhibin.

40. The DNA plasmid of claim 39 wherein the inducible promoter is from mouse alpha inhibin.

41. The DNA plasmid of claim 37 wherein the inducible promoter is selected from a drug inducible tetracycline responsive promoter.

42. The plasmid pIK6.1 MIP(α)-E4 ORF6 designated ^{adeno} ATCC # 


43. A DNA plasmid comprising an adenoviral gene E2A operably linked to an inducible promoter.

44. The DNA plasmid of claim 43 wherein the inducible promoter is a promoter selected from the cAMP response element binding protein regulated genes.

5 45. The DNA plasmid of claim 44 wherein the inducible promoter is selected from the gene encoding mammalian alpha inhibin.

10 46. The DNA plasmid of claim 45 wherein the inducible promoter is from mouse alpha inhibin.

47. The DNA plasmid of claim 45 wherein the inducible promoter is a drug inducible tetracycline responsive promoter.

15 48. The plasmid *adms* pIK6.1 MIP(α)-E2A designated ATCC


20 49. A packaging cell line that supports the growth of a mutant adenovirus defective in replication or a recombinant adenoviral vector, wherein said adenovirus or adenoviral vector comprises at least two deletions, at least two mutations, or at least one mutation and one deletion selected from the group consisting of E1, E2A, E4-ORF6 early regions, and optionally a deletion of the E3 gene region and said recombinant adenoviral vector additionally comprises a transgene that replaces any one of said deletions.

25 50. A packaging cell line that supports the growth of a mutant adenovirus defective in replication or a recombinant adenoviral vector, wherein said adenovirus or adenoviral vector comprises two deletions from the E1 and E4-ORF6 early gene regions, and optionally a deletion of the

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5 E3 gene region and said recombinant adenoviral vector additionally comprises a transgene that replaces any one of said deletions.

51. The packaging cell line derived from human embryonic kidney cells transfected with the adenovirus 5 E4 ORF6 DNA gene fragment designated #CRL . *adman*

10 52. A packaging cell line that supports the growth of a mutant adenovirus defective in replication or a recombinant adenoviral vector, wherein said adenovirus or adenoviral vector comprises two deletions from the E1 and E2A early gene regions, and optionally a deletion of the E3 gene region and said recombinant adenoviral vector
15 additionally comprises a transgene that replaces any one of the deletions.

20 53. A DNA plasmid comprising one or more adenoviral late gene regions operably linked to a tetracycline responsive promoter.

25 54. The DNA plasmid of claim 53 wherein said adenoviral late gene region is selected from L1, L2, L3, L4 or L5.

30 55. A recombinant adenoviral vector, wherein said vector comprises two deletions from the E1 and E4 early gene regions, and optionally a deletion of the E3 gene region, and further wherein said recombinant adenoviral vector additionally comprises a transgene that replaces any of said deletions.

56. A mutant adenovirus defective in replication, wherein said adenovirus comprises two deletions from the E1 and E4 early regions, and optionally a deletion of the E3 region.

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57. A recombinant adenoviral vector, wherein said vector comprises three deletions from the E1, E2A and E4 early gene regions, and optionally a deletion of the E3 gene region, and further wherein said recombinant adenoviral vector additionally comprises a transgene that replaces any of said deletions.

10

58. A mutant adenovirus defective in replication, wherein said adenovirus comprises three deletions from the E1, E2A and E4 early regions, and optionally a deletion of the E3 region

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59. A recombinant adenoviral vector, wherein said vector comprises two deletions from the E1 and E2A early gene regions, and optionally a deletion of the E3 gene region, and further wherein said recombinant adenoviral vector additionally comprises a transgene that replaces any of said deletions.

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60. A mutant adenovirus defective in replication, wherein said adenovirus comprises two deletions from the E1 and E2A early regions, and optionally a deletion of the E3 region.

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61. The recombinant adenoviral vector of claim 21, 22, 36, 55, 57 or 59 wherein said transgene is expressed under the control of the human phosphoglycerate kinase promoter.

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62. The recombinant adeno-associated viral vector of claim 26 or 28 wherein said transgene is expressed under the control of the human phosphoglycerate kinase promoter.